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Interlaboratory Evaluation of Cellulosic Acid-soluble Internal Air Sampling Capsules for Multi-element Analysis

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Abstract

An interlaboratory study was carried out to evaluate the use of acid-soluble cellulosic air sampling capsules for their suitability in the measurement of trace elements in workplace atmospheric samples. These capsules are used as inserts to perform closed-face cassette sample collection for occupational exposure monitoring. The interlaboratory study was performed in accordance with NIOSH guidelines that describe statistical procedures for evaluating measurement accuracy of air monitoring methods. The performance evaluation materials used consisted of cellulose acetate capsules melded to mixed-cellulose ester filters that were dosed with multiple elements from commercial standard aqueous solutions. The cellulosic capsules were spiked with the following 33 elements of interest in workplace air monitoring: Ag, Al, As, Ba, Be, Ca, Cd, Co, Cr, Cu, Fe, In, K, La, Li, Mg, Mn, Mo, Ni, P, Pb, Sb, Se, Sn, Sr, Te, Ti, Tl, V, W, Y, Zn, Zr. The elemental loading levels were certified by an accredited provider of certified reference materials. Triplicates of media blanks and multielement-spiked capsules at three different elemental loadings were sent to each participating laboratory; the elemental loading levels were not revealed to the laboratories. The volunteer participating laboratories were asked to prepare the samples by acid dissolution and to analyze aliquots of extracted samples by inductively coupled plasma atomic emission spectrometry in accordance with NIOSH methods. It was requested that the study participants report their analytical results in units of μg of each target element per internal capsule sample. For the majority of the elements investigated (30 out of 33), the study accuracy estimates obtained satisfied the NIOSH accuracy criterion (A < 25%). This investigation demonstrates the utility of acid-soluble internal sampling capsules for multielement analysis by atomic spectrometry.

Keywords

aerosol sampling; internal capsule; elemental analysis; occupational hygiene

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INTRODUCTION

Airborne particles that are collected using closed-face filter cassettes (CFCs), which are used widely to sample workplace aerosols, can deposit in places other than on the filter, most notably on the inside walls of the cassette.[1] If only the filter is then analyzed, these particulate wall deposits will not be included in the ensuing elemental analysis, potentially leading to underestimation of exposure.[2] An effective technique for ensuring that internal non-filter deposits are included in the analysis is to collect airborne particles within an acid-soluble internal capsule which, following sampling, can be dissolved along with the filter for subsequent elemental analysis.[3] In this project, an interlaboratory study (ILS) was carried out to evaluate the use of cellulosic CFC internal capsules for their suitability in the determination of trace elements in airborne samples from workplaces.

The overall goal of this effort was to evaluate and validate a method that accounts for all aerosol particles entering the inlet of the CFC sampler, thereby including material that would not otherwise be measured by filter-only analysis procedures. A principal aim of this work was to carry out an ILS to evaluate the analytical suitability of cellulosic internal capsules for their use with traditional plastic air sampling cassettes. In an effort to complement previously-reported results for soluble internal capsules fortified with fewer metals and metalloids,[3] it was deemed important to obtain performance data for many more elements that are of concern for workplace exposure monitoring. The ILS entailed fortifying the cellulosic capsules with various loadings of metals and metalloids of interest and sending them to volunteer laboratories for analysis. The capsules were subjected to acid dissolution and analyzed by the participating laboratories for their elemental content by inductively coupled plasma – atomic emission spectrometry (ICP-AES). The use of cellulosic internal capsules is meant to replace the practice of filter-only based sample collection and subsequent analysis using CFCs, as applicable.

METHODS

The materials evaluated in this investigation were Solu-Sert™ cellulosic acid-soluble capsules, which consisted of cellulose acetate capsules attached to 37-mm, 0.8 μm pore size mixed-cellulose ester (MCE) filters (Zefon International, Ocala, FL). The schematic for sample collection using an internal capsule is illustrated in Figure 1. The Solu-Sert capsules were spiked with 33 elements of interest by High-Purity Standards (Charleston, SC), an accredited provider of environmental certified reference materials (CRMs). Spiking of Solu-Sert capsules was carried out using standard solutions (containing the elements of interest) traceable to national standards, i.e., National Institute of Standards and Technology (NIST, Gaithersburg, MD). Spikes were prepared in order to produce CRMs having desired loading levels of the metals and metalloids of concern in occupational exposure assessment (Table I). Certificates of analysis for the CRMs, provided by the vendor, listed certified reference values for each element at each loading level. The target loading levels and identities of the 33 elements within the samplers (Table I) were chosen based upon reasonable assumptions of what a variety of laboratories could confidently measure and considering previous validation of related NIOSH ICP-AES methods (e.g., NIOSH methods 7300, 7301, 7302, 7303).[4-7]

Triplicates of Solu-Sert capsules spiked at each loading level, plus media blanks (also in triplicate), were conveyed to each participant; loading levels were unknown to the participants. Sampling chain-of-custody procedures were followed throughout the ILS, in accordance with ASTM D4840.[8] The Solu-Sert CRMs were sent to the volunteer participating laboratories by express mail. Laboratories that participated in the ILS and reported analytical results included: CDC/NIOSH, Cincinnati, OH; Occupational Safety and Health Administration (OSHA) Salt Lake Technical Center, Sandy, UT; Bureau Veritas North America (BVNA), Novi, MI; ALS Laboratories, Salt Lake City, UT; Institut National de Recherche et de Sécurité (INRS), Vandoeuvre-lès-Nancy, France; Forensic Analytical Services, Hayward, CA; BWXT Y-12 National Security Organization, Oak Ridge, TN; and the Wisconsin Occupational Health Laboratory (WOHL), Madison, WI. The participating laboratories were asked to prepare the Solu-Sert CRM samples by acid dissolution and to analyze aliquots of extracted samples for multielemental analysis by ICP-AES in accordance with applicable NIOSH 7300-series methods.[4-7]

The sample preparation methods used by the participating laboratories are summarized in Table II. Five participating laboratories used hot block extraction, two used hot plate digestion, and two used microwave digestion. One of the above laboratories used two different procedures, where hot plate or microwave digestion was used on separate sets of Solu-Sert CRMs. For the purposes of the ILS, results from these two different sample dissolution procedures from the same laboratory were treated as being from separate laboratories. For data presentation, laboratories are identified by code to maintain confidentiality. The participating laboratories were requested to report their results in units of micrograms per sample of each element analyzed.

RESULTS

Reported results from the participating laboratories are presented in Table IIIa for media blanks; laboratory-reported results that were below the estimated method detection limit (MDL) or reporting limit (RL) are indicated by a (<) sign in table entries, with the MDL or RL value listed in each instance. The MDL or RL values were reported in accordance with the participating laboratory's usual procedure. Mean laboratory-reported results from individual laboratories are presented in Tables IIIb-d for three different Solu-Sert™ CRM elemental loadings, i.e., Levels 1 (low), 2 (medium) and 3 (high). Not all laboratories reported results for all elements. Some laboratories reported results above the MDL, while others only reported results above the particular laboratory's RL.

Mean overall laboratory-reported results and standard deviations from the ILS are shown in Table IVa for media blanks; only those results from laboratories reporting data above the MDL or RL are shown. Overall ILS mean laboratory results are shown in Tables IVb-d for the three different Solu-Sert CRM elemental loadings, i.e., Levels 1 (low loading), 2 (medium loading) and 3 (high loading). Also for each loading level, standard deviations, relative standard deviations and recoveries, the latter computed with respect to CRM reference values, are presented in Tables IVb-d. Calculations were performed before the results were rounded to 3 significant figures. For a few of the data sets in Tables IVb-d,

outliers (identified by means of Grubbs' test at 1% confidence level) were removed prior to carrying out subsequent statistical computations.

Estimates of bias, precision and accuracy, computed statistically in accordance with established NIOSH guidelines,[9, 10] are presented in Table V. For each data subset, Grubbs' test at the 1% confidence level was used to identify outliers which, if identified, were removed prior to further statistical calculations. Bias, precision and accuracy estimates were computed based on results from all three Solu-Sert loading levels. All calculations were based on the original raw data (and not the mean laboratory results presented in Tables IIIb-d). Analysis of Variance procedure was used to test for homogeneity of bias; Bartlett's was used for testing homogeneity of RSD (precision) on the data sets for each element. Where results were homogeneous across spiking levels, pooled estimates of bias and precision were used to compute method accuracy for each element. If homogeneity tests failed to pass, the most conservative, i.e., largest, estimates of precision and bias were used to estimate accuracy for each element. It must be pointed out that the accuracy estimates presented in Table V also include a conservative imprecision component of ±5% sampling pump error, in accordance with recommended guidelines.[9]

DISCUSSION

The laboratory-reported data shown in Tables III and IV demonstrated no statistically significant differences due to the chosen sample preparation procedure. Using SAS Mixed model procedure, statistical tests of data subsets for heating method (hot plate, hot block or microwave) and acid mixture sample treatment yielded no statistically significant differences in the reported multielement analysis results at 5% significance level ($p=0.23$ for heating method, $p=0.73$ for acid mixure). The test factors included heating method, acid mixture, level and element as the fixed factor and lab and sample nested with lab and level as the random factors. The interactions of heating method with element and acid mixture with element were also included. Thus the implication is that, for the Solu-Sert samples evaluated, the various sample preparation procedures performed equivalently. These results are consistent with previous reports entailing elemental analysis of soluble capsules for use as cassette inserts.[3, 11]

While no statistically significant differences were found based upon the sample preparation procedures used by the labs, it is important to note that lab-to-lab differences were taken into account in those calculations. Some limitations in the sample preparation methods for certain elements may have been found to be statistically significant had it not been necessary to consider interlaboratory variations. The presence and identity of outliers may prove valuable in identifying potentially problematic elements for certain sample preparation methods. Of particular importance are the less than quantitative (<90%) recoveries for Sb, Sn, and Ti using the hot plate method of Lab 2a (Table III). This particular sample preparation method may not be amenable to the analysis of Sb, Sn and Ti. Also, certain elements (e.g., Sn) may require the presence of additional acids (beyond nitric) to maintain stability in solution.

It can be seen from the reference values listed in Table IVa that appreciable media background levels were found for several elements, notably Al, Ca, Cr, Fe, K, and Mg. Trace media background levels of a few other elements, i.e., Ba, Cu and Zn, were also obtained. Additionally, media background levels > 0.5 μg for In, P, Sb, Se, and Tl were reported by the laboratories. However, it is noted that only a few laboratories had MDLs or RLs low enough to report measurable elemental analysis results for media blanks (Table IVa). For Levels 1, 2 and 3, the reported results for laboratory means compared to certified values yielded quantitative recoveries (i.e., within 100% ± 10% of the reference value) for the vast majority of elements and spike levels (Tables IVb-d). Mean overall recoveries below 90% were found only for Cr, K, and W at low loadings, for Ag at medium and high spike levels and for In at the high spike level. Significant media background levels reported for certain elements did not negatively affect recoveries. While there was measurable background for certain elements (mentioned above; see Table IVa), these background levels were effectively corrected for during analysis, as evidenced by the quantitative recoveries obtained for the vast majority of elements and loading levels (Tables IVb-d). Most values for precision (expressed as relative standard deviation, RSD) were <0.20 (Tables IVb-d), which compare favorably with the variability typically observed in interlaboratory multielement analysis of air filter samples by atomic spectrometric methods.[12] The results for accuracy summarized in Table V generally demonstrate the suitability of Solu-Sert capsules for multielement analysis by acid dissolution and ICP-AES. The mean accuracy estimate is ≥0.25 for only two elements: Ag and In. The upper 95% confidence limit for the accuracy estimate exceeds 0.25 for only three elements: Ag, In and Sn. Bias estimates beyond ±0.10 are obtained only for two elements: Ag and In. Estimates of precision and overall precision are >0.10 for only one element: Sn. For 30 of the 33 elements evaluated, accuracy estimates of 0.25 or less demonstrate that the method using soluble capsules is valid for quantitative multielement analytical determination.

Difficulties with atomic spectrometric interlaboratory analysis of Ag on air filter samples have been observed previously.[12] Since Ag^+ ions are light-sensitive and subject to photoreduction, it is recommended to carry out sample preparation in light-protected vessels if this element is to be analyzed.[13] Also, precipitation of AgCl in chloride-containing solutions is possible and should be considered. ILS results reported here for In (Table V) are unfortunately limited since many participants did not report results for this element. It is anticipated that better estimates for In (tighter precision and lesser bias) would be obtained with a larger number of participating laboratories. The somewhat higher estimates for ILS variability and accuracy for Sn (Table V) may be improved with data from additional laboratory participants,[14] especially for low-level samples.

In summary, this study has served to validate the use of acid-soluble internal capsules for CFC sampling and multielement analysis of workplace air samples; therefore, the use of appropriately-fitted soluble aerosol-collection capsules is suitable for elemental sampling and analysis. For the majority of the elements investigated, interlaboratory precision and recovery estimates from the participating laboratories amply demonstrated the utility of the cellulosic internal capsules for the measurement of trace elements of interest in occupational monitoring. Of the 33 elements evaluated in the ILS, 30 were found to satisfy the NIOSH criterion for method accuracy. Based on this work and the results of related laboratory and

field studies,[3,11] a new NIOSH procedure (Method no. 7306) will soon be promulgated describing the use of soluble cassette inserts for sampling and analysis of metals and metalloids in workplace atmospheres.

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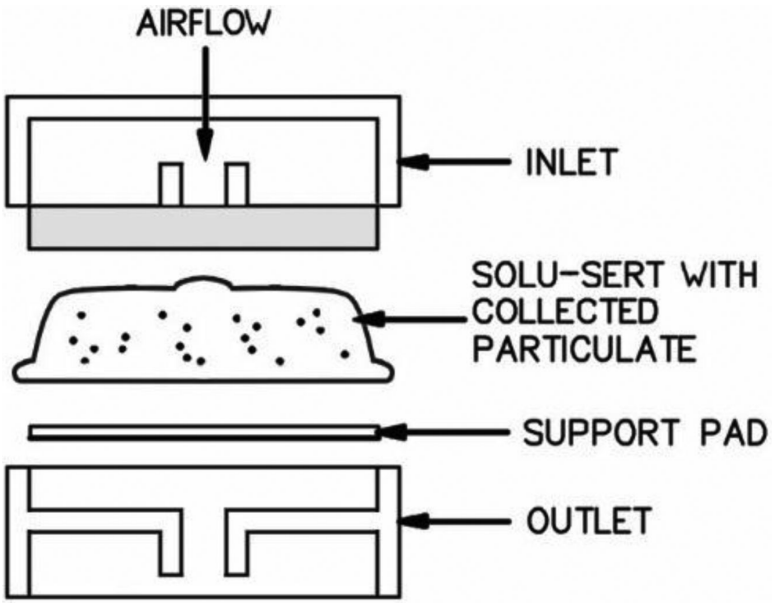

FIGURE 1.
Schematic of closed-face filter (CFC) aerosol sample collection using an internal filter capsule. (Used with permission of Zefon International, Inc.)

TABLE I

Elements and nominal spiking levels (in μg) in soluble capsules

Element (Symbol)	Level 1 (Low level)	Level 2 (Medium level)	Level 3 (High level)
Silver (Ag)	5.02 ± 0.1	10.1 ± 0.2	20.1 ± 0.4
Aluminum (Al)	10.0 ± 0.2	30.3 ± 0.6	60 ± 1
Arsenic (As)	5.0 ± 0.1	20.2 ± 0.4	40.1 ± 0.8
Barium (Ba)	2.01 ± 0.04	7.1 ± 0.1	15.0 ± 0.3
Beryllium (Be)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Calcium (Ca)	100 ± 2	151 ± 3	201 ± 4
Cadmium (Cd)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Cobalt (Co)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Chromium (Cr)	2.01 ± 0.04	7.0 ± 0.1	14.9 ± 0.3
Copper (Cu)	3.02 ± 0.06	14.9 ± 0.3	29.7 ± 0.6
Iron (Fe)	20.1 ± 0.4	39.8 ± 0.8	79 ± 2
Indium (In)	5.04 ± 0.05	14.9 ± 0.1	39.7 ± 0.4
Potassium (K)	10.0 ± 0.2	15.1 ± 0.3	20.1 ± 0.4
Lanthanum (La)	3.01 ± 0.03	10.1 ± 0.1	20.1 ± 0.2
Lithium (Li)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Magnesium (Mg)	10.0 ± 0.1	25.2 ± 0.3	100 ± 1
Manganese (Mn)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Molybdenum (Mo)	2.01 ± 0.02	7.1 ± 0.1	15.0 ± 0.2
Nickel (Ni)	2.01 ± 0.02	7.0 ± 0.1	14.9 ± 0.1
Phosphorus (P)	10.1 ± 0.2	24.9 ± 0.5	99 ± 2
Lead (Pb)	10.0 ± 0.2	25.2 ± 0.5	100 ± 2
Antimony (Sb)	5.0 ± 0.1	25.1 ± 0.5	40.2 ± 0.8
Selenium (Se)	3.0 ± 0.2	15.1 ± 0.3	30 ± 2
Tin (Sn)	2.01 ± 0.04	7.0 ± 0.1	14.9 ± 0.3
Strontium (Sr)	2.01 ± 0.02	7.1 ± 0.1	15.0 ± 0.2
Tellurium (Te)	3.02 ± 0.06	12.6 ± 0.3	20.1 ± 0.4
Titanium (Ti)	2.01 ± 0.04	7.0 ± 0.1	14.9 ± 0.3
Thallium (Tl)	3.01 ± 0.06	10.1 ± 0.2	20.1 ± 0.4
Vanadium (V)	3.02 ± 0.06	7.0 ± 0.1	14.9 ± 0.3
Tungsten (W)	10.1 ± 0.2	25.1 ± 0.5	40.2 ± 0.8
Yttrium (Y)	2.01 ± 0.04	7.1 ± 0.1	15.0 ± 0.3
Zinc (Zn)	5.0 ± 0.1	24.9 ± 0.5	59 ± 1
Zirconium (Zr)	2.01 ± 0.04	7.0 ± 0.1	14.9 ± 0.3

TABLE II

Sample preparation methods used by laboratories participating in the interlaboratory study

Laboratory No.	Sample dissolution procedure
1	hot block extraction; HNO_3, 90-95 °C (NIOSH 7303)
2a	hot plate digestion; $HNO_3/HClO_4$, 120-130 °C (NIOSH 7300)
2b	microwave digestion; HNO_3, 150 °C (NIOSH 7302)
3	hot block extraction; HNO_3/HCl, 95 °C (NIOSH 7303)
4	microwave digestion; HNO_3/H_2O_2, 210 °C (modified NIOSH 7302)
5	hot block extraction; HNO_3, 95 °C (NIOSH 7303)
6	hot block extraction; HNO_3/HCl, 95 °C (NIOSH 7303)
7	hot block extraction; HNO_3/HCl, 95 °C (NIOSH 7303)
8	hot plate digestion; $HNO_3/H_2SO_4/H_2O_2$, 120-130 °C (modified NIOSH 7300)

TABLE IIIa

Soluble capsules interlaboratory study – Elemental determination by ICP-AES: Individual mean laboratory media blank results (μg/sample)

Element	Lab 1 (RL)[A]	Lab 2a (MDL)[B]	Lab 2b (MDL)	Lab 3 (MDL)	Lab 4 (MDL)	Lab 5 (RL)	Lab 6 (RL)	Lab 7 (RL)	Lab 8 (RL)
Ag	<0.250[C]	<0.017	0.060	<0.03	<4.2	<0.15	< 0.5	< 0.3	NA[D]
Al	<5.00	2	1.3	<2	0.584	<10	< 5	NA	NA
As	<2.50	0.10	0.782	<2	<0.83	<0.75	< 5	< 0.6	NA
Ba	<0.250	0.218	0.265	<0.6	0.269	0.26	0.184	< 0.5	NA
Be	<0.0130	<0.0040	<0.0090	0.0085	<0.0053	<0.013	< 0.012	< 0.08	<0.1
Ca	<15.0	15.3	15.5	<3	11.6	25	15.0	20	NA
Cd	<0.0750	<0.22	0.0252	<0.03	<0.022	<0.25	<0.25	< 0.6	<0.5
Co	<0.0750	<0.0099	0.0341	<0.03	<0.049	<0.25	< 0.5	< 0.3	<2.5
Cr	<1.30	0.318	0.533	<0.4	0.92	<4	0.503	< 0.9	<10
Cu	<0.500	0.231	0.12	<0.8	<0.042	<1.5	< 0.5	< 0.5	<2.5
Fe	<5.00	1.2	2.38	1.4	1.48	<5	1.29	< 20	<25
In	NA	<0.11	0.673	<0.3	<0.17	NA	NA	< 0.6	NA
K	<13.0	2	1.04	<6	<0.15	<7.5	< 50	NA	NA
La	NA	<0.047	0.200	<0.02	<0.016	NA	NA	NA	NA
Li	<0.500	<0.019	0.0078	<0.02	<0.0059	<0.5	< 0.25	NA	NA
Mg	<1.40	2.47	3.30	<1	2.51	5.1	< 5	NA	NA
Mn	<0.130	<0.012	<0.020	0.032	<0.0285	<0.25	< 0.12	< 0.8	<2.5
Mo	<0.380	0.013	0.0687	<0.1	<0.12	<0.5	< 0.5	< 2	<25
Ni	<0.130	0.0351	0.145	0.1	<0.28	<1	< 1.2	< 0.3	<25
P	<5.00	0.57	2.00	<2	<0.49	NA	< 12	NA	NA
Pb	<1.30	<0.40	0.377	<1	0.063	<1.8	< 2.5	< 0.8	<5
Sb	<1.50	<0.7	0.561	<1	<0.41	<1.5	< 5	< 0.5	<25
Se	<2.50	0.060	1.06	<5	<0.675	<1.3	< 5	< 0.9	NA
Sn	<2.50	<0.2	0.413	<0.4	<0.14	<5	< 0.12	< 30	NA
Sr	<0.380	0.0423	0.0516	0.0095	0.0408	<0.15	NA	NA	NA
Te	<1.30	0.1	0.697	<0.6	<0.43	NA	NA	NA	NA
Ti	<0.0750	0.032	0.0968	0.022	0.0935	<0.5	< 1.2	NA	NA
Tl	<1.30	<0.025	0.402	1.1	NA	<2.5	< 5	< 3	NA
V	<0.230	<0.011	0.0429	<0.02	<0.025	<0.25	< 0.5	< 0.5	<1.5
W	<1.30	<0.43	0.163	<0.1	<0.30	NA	NA	NA	NA
Y	<0.0750	<0.0083	0.016	0.012	<0.0053	NA	NA	NA	NA
Zn	<0.500	<0.74	0.262	0.47	<0.089	<1.8	< 1.2	< 0.8	<25
Zr	<0.500	<0.072	0.0475	0.037	0.021	NA	< 5	NA	NA

[A] RL: reporting limit

[B] MDL: method detection limit

[C] < sign: results below reporting limit or method detection limit

[D] NA: not applicable: not reported by the laboratory

TABLE IIIb

Soluble capsules interlaboratory study – Elemental determination by ICP-AES: Level 1 individual mean laboratory results (μg/sample)

Element	Lab 1	Lab 2a	Lab 2b	Lab 3	Lab 4	Lab 5	Lab 6	Lab 7	Lab 8
Ag	4.91	4.47	4.80	5.43	<4.2[C]	4.93	3.01	5.07	NA[D]
Al	9.96	10.5	11.1	9.33	9.42	10.3	10.4	NA	NA
As	4.80	4.67	5.64	4.87	4.57	5.17	<5	5.10	NA
Ba	2.03	2.12	2.15	1.80	2.41	2.30	2.14	2.20	NA
Be	1.98	1.94	2.14	2.03	2.17	2.07	1.91	2.00	1.99
Ca	98.9	109	115	73.0	111	127	109	130	NA
Cd	1.98	1.87	2.08	2.00	2.04	2.10	2.03	2.10	2.09
Co	2.02	1.84	2.17	2.00	2.07	2.33	2.02	2.20	2.06
Cr	2.12	2.23	2.91	1.60	2.45	<4	2.42	2.53	2.42
Cu	3.13	4.08	3.30	2.93	3.07	3.17	3.13	3.17	3.40
Fe	20.9	20.8	24.0	21.3	22.3	31.0	20.9	20.0	24.6
In	NA	4.79	6.32	5.10	4.62	NA	NA	2.20	NA
K	<13.0	12.3	11.8	9.30	3.80	10.0	<50	NA	NA
La	NA	2.81	3.36	2.90	3.12	NA	NA	NA	NA
Li	2.01	1.74	1.64	1.80	1.85	2.07	1.99	NA	NA
Mg	9.40	11.4	13.1	9.97	13.0	14.7	12.0	NA	NA
Mn	2.00	1.93	1.65	2.10	2.18	2.10	1.97	2.03	2.07
Mo	2.06	1.85	2.27	1.93	2.01	2.13	1.92	2.00	2.03
Ni	2.12	1.90	2.51	2.03	2.20	2.07	2.01	2.47	2.28
P	10.1	9.80	12.1	10.6	9.93	NA	<12	NA	NA
Pb	10.2	9.16	11.1	10.0	9.58	9.90	9.66	11.0	10.2
Sb	4.83	4.49	5.59	4.90	5.17	4.87	<5	5.07	4.72
Se	3.01	2.66	4.09	<5	3.29	3.63	<5	3.53	NA
Sn	<2.50	2.02	2.58	2.03	1.30	<5	2.01	<30	NA
Sr	2.00	1.99	2.09	2.00	2.29	2.00	NA	NA	NA
Te	2.89	2.77	4.02	3.30	2.68	NA	NA	NA	NA
Ti	2.00	1.98	2.28	2.03	2.18	2.23	2.06	NA	NA
Tl	2.99	2.77	3.40	3.23	NA	3.03	<5	3.00	NA
V	3.02	3.05	3.32	3.00	3.06	3.23	2.95	2.70	3.05
W	7.85	6.98	9.57	8.70	8.83	NA	NA	NA	NA
Y	2.05	1.91	2.12	2.00	2.05	NA	NA	NA	NA
Zn	5.13	5.24	5.66	5.10	4.73	5.50	5.01	5.07	5.65
Zr	1.95	2.00	2.19	1.90	2.14	NA	<5	NA	NA

[C] < sign: results below reporting limit or method detection limit

[D] NA: not applicable: not reported by the laboratory

TABLE IIIc

Soluble capsules interlaboratory study – Elemental determination by ICP-AES: Level 2 individual mean laboratory results (μg/sample)

Element	Lab 1	Lab 2a	Lab 2b	Lab 3	Lab 4	Lab 5	Lab 6	Lab 7	Lab 8
Ag	10.1	9.12	9.85	5.70	<4.2[C]	9.40	4.93	9.97	NA[D]
Al	30.1	29.3	29.4	28.0	29.4	31.0	29.7	NA	NA
As	20.3	18.9	22.6	20.7	21.5	21.3	20.2	21.0	NA
Ba	7.17	6.77	7.11	6.90	8.31	7.27	7.15	7.17	NA
Be	7.01	6.41	7.55	7.00	7.98	7.03	6.57	7.13	6.77
Ca	152	159	171	110.	169	180.	158	187	NA
Cd	7.01	6.55	7.27	7.10	7.59	6.90	6.90	7.07	7.07
Co	7.10	6.55	6.99	7.00	7.66	7.77	6.83	7.37	6.80
Cr	7.28	7.34	8.09	6.90	8.78	7.60	7.64	7.37	7.45
Cu	15.7	14.6	15.9	15.0	16.0	15.0	14.8	14.3	15.7
Fe	42.1	39.9	42.4	41.7	46.2	45.7	40.6	40.0	44.1
In	NA	14.2	17.0	15.0	14.3	NA	NA	7.20	NA
K	15.4	19.8	17.7	14.3	9.10	16.0	<50	NA	NA
La	NA	9.53	10.8	9.93	11.2	NA	NA	NA	NA
Li	7.09	6.52	5.73	6.50	6.85	7.03	6.79	NA	NA
Mg	23.9	26.2	28.9	26.0	31.0	30.0	26.8	NA	NA
Mn	7.06	6.41	7.16	7.07	8.01	6.97	6.74	6.93	6.90
Mo	7.59	6.72	7.75	7.20	7.66	7.37	6.95	7.00	7.17
Ni	7.47	6.47	7.35	7.17	8.21	6.97	6.79	7.87	7.02
P	25.6	21.5	28.2	26.3	27.2	NA	25.3	NA	NA
Pb	26.0	23.3	26.5	26.0	27.1	25.0	24.3	26.0	23.5
Sb	24.8	22.4	26.3	25.7	27.3	24.3	24.1	24.7	24.1
Se	14.9	14.2	18.6	15.7	17.7	17.0	16.4	17.0	NA
Sn	6.89	4.60	8.22	6.77	7.10	7.10	NA	<30	NA
Sr	7.12	6.58	7.38	7.13	8.33	7.07	6.94	NA	NA
Te	12.6	11.6	14.1	13.7	12.8	NA	NA	NA	NA
Ti	7.12	5.56	7.56	7.00	7.74	7.57	6.93	NA	NA
Tl	9.76	9.37	11.1	9.80	NA	9.83	10.6	10.0	NA
V	7.20	6.95	7.83	7.07	7.60	7.37	6.74	6.40	6.89
W	24.3	20.4	25.4	24.3	28.2	NA	NA	NA	NA
Y	7.32	6.54	7.33	7.13	7.70	NA	NA	NA	NA
Zn	25.9	23.8	25.9	25.0	27.6	25.3	24.1	24.3	26.7
Zr	6.97	6.14	7.60	6.63	7.82	NA	6.63	NA	NA

[C] < sign: results below reporting limit or method detection limit

[D] NA: not applicable: not reported by the laboratory

TABLE IIId

Soluble capsules interlaboratory study – Elemental determination by ICP-AES: Level 3 individual mean laboratory results (μg/sample)

Element	Lab 1	Lab 2a	Lab 2b	Lab 3	Lab 4	Lab 5	Lab 6	Lab 7	Lab 8
Ag	19.9	17.0	19.3	7.70	<4.2[C]	9.63	2.45	20.0	NA[D]
Al	59.5	57.1	57.2	59.7	56.8	60.0	59.3	NA	NA
As	40.7	35.6	43.2	41.3	41.1	43.0	40.2	41.3	NA
Ba	15.3	14.2	14.7	15.0	16.8	15.3	15.1	15.0	NA
Be	15.1	13.7	15.2	15.0	16.5	15.0	14.2	15.0	14.6
Ca	199	196	219	150.	211	230.	206	237	NA
Cd	15.0	13.2	15.2	15.3	15.8	15.0	14.8	15.3	15.3
Co	15.4	13.4	15.2	15.3	15.8	16.3	14.7	16.0	14.7
Cr	15.3	14.5	16.0	15.3	16.4	15.3	15.2	15.0	15.2
Cu	31.5	28.3	30.8	30.0	30.1	30.0	29.5	29.0	30.4
Fe	83.4	73.8	84.7	84.3	86.2	88.3	80.0	80.0	87.0
In	NA	35.3	42.0	41.3	37.5	NA	NA	15.0	NA
K	21.4	28.7	24.0	20.7	15.3	21.3	<50	NA	NA
La	NA	17.9	21.1	20.0	21.4	NA	NA	NA	NA
Li	15.4	14.7	13.1	15.3	14.8	15.0	14.5	NA	NA
Mg	95.4	92.6	109	110.	109	110.	101	NA	NA
Mn	15.1	13.2	15.5	15.0	16.4	15.0	14.5	15.0	14.6
Mo	16.0	13.8	16.3	15.7	15.6	16.0	14.9	14.7	14.9
Ni	16.0	13.3	15.6	15.3	16.8	15.0	14.5	16.7	15.0
P	100.	77.1	101	103	102	NA	99.0	NA	NA
Pb	103	88.0	103	110.	103	98.7	98.7	107	89.7
Sb	40.0	29.1	40.9	42.0	42.5	39.0	38.7	39.7	38.9
Se	29.9	25.2	35.6	29.3	32.4	33.0	32.0	33.3	NA
Sn	15.0	1.42	16.6	15.3	14.7	15.0	NA	<30	NA
Sr	15.1	13.9	14.8	15.3	17.0	15.0	14.8	NA	NA
Te	19.9	16.5	21.9	23.0	19.8	NA	NA	NA	NA
Ti	15.1	6.53	15.6	15.0	15.9	16.0	14.7	NA	NA
Tl	19.6	17.1	21.4	21.0	NA	19.0	20.6	19.7	NA
V	15.5	14.1	16.6	15.3	15.7	16.0	14.5	14.0	15.0
W	38.8	27.9	43.5	40.3	43.2	NA	NA	NA	NA
Y	15.6	13.9	15.2	15.0	15.8	NA	NA	NA	NA
Zn	61.7	54.9	60.3	60.3	63.5	60.3	57.8	58.3	64.4
Zr	14.9	8.60	15.5	14.0	16.0	NA	14.1	NA	NA

[C] < sign: results below reporting limit or method detection limit

[D] NA: not applicable: not reported by the laboratory

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TABLE IVa

Blank soluble capsule media – Mean ILS results & certified reference values

Element	No. Labs[E]	Mean[F] (μg)	Std. Dev.[G] (μg)	Reference value (μg)[H]
Ag	1	0.060	-	<0.01
Al	3	1.1	0.49	0.6
As	2	0.44	0.48	<0.01
Ba	5	0.24	0.037	0.2
Be	1	0.0085	-	<0.01
Ca	6	17	4.6	14
Cd	1	0.025	-	<0.01
Co	1	0.034	-	<0.01
Cr	4	0.57	0.25	0.9
Cu	2	0.18	0.077	0.14
Fe	5	1.5	0.48	1.2
In	1	0.67	-	<0.01
K	2	1.4	0.44	0.6
La	1	0.20	-	<0.01
Li	1	0.0078	-	<0.01
Mg	4	3.3	1.2	2.7
Mn	1	0.032	-	<0.01
Mo	2	0.041	0.039	<0.01
Ni	3	0.093	0.055	<0.01
P	2	1.3	1.0	<0.01
Pb	2	0.22	0.22	<0.01
Sb	1	0.56	-	<0.01
Se	2	0.56	0.70	<0.01
Sn	1	0.41	-	<0.01
Sr	4	0.036	0.018	<0.01
Te	2	0.40	0.43	<0.01

Element	No. Labs[E]	Mean[F] (µg)	Std. Dev.[G] (µg)	Reference value (µg)[H]
Ti	4	0.061	0.039	<0.01
Tl	2	0.73	0.46	<0.01
V	1	0.043	-	<0.01
W	1	0.16	-	<0.01
Y	2	0.014	0.0033	<0.01
Zn	2	0.37	0.15	0.2
Zr	3	0.035	0.014	<0.01

[E] Number of laboratories reporting at least one result >MDL (or RL)

[F] values based only on reported results above MDL (or RL);

[G] standard deviation (if $p>1$);

[H] as reported by the CRM provider

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TABLE IVb

Soluble capsules ILS mean values vs. certified reference values – Level 1

Element	No. Labs[E]	Mean(μg)	Std. Dev. (μg)[G]	RSD[I]	Reference value (μg)[H]	Recovery (%)
Ag	7	4.66	0.78	0.168	5.0	93.2
Al	7	10.1	0.62	0.061	10.6	95.7
As	7	4.97	0.36	0.073	5.0	99.4
Ba	8	2.14	0.18	0.084	2.21	97.0
Be	9	2.03	0.09	0.044	2.01	100.8
Ca	8	109.	17.70	0.162	114	95.8
Cd	9	2.03	0.07	0.036	2.01	101.1
Co	9	2.08	0.14	0.068	2.01	103.4
Cr	8	2.33	0.38	0.161	2.91	80.2
Cu	8[J]	3.16	0.14	0.045	3.16	100.1
Fe	9	22.9	3.41	0.149	21.3	107.4
In	5	4.61	1.50	0.326	5.0	92.1
K	5	9.44	3.39	0.359	10.6	89.0
La	4	3.05	0.25	0.081	3.01	101.3
Li	7	1.87	0.16	0.085	2.01	93.0
Mg	7	11.9	1.85	0.155	12.7	93.9
Mn	9	2.01	0.15	0.076	2.01	99.8
Mo	9	2.02	0.13	0.062	2.01	100.7
Ni	9	2.18	0.21	0.096	2.01	108.2
P	5	10.5	0.94	0.090	10.1	103.9
Pb	9	10.1	0.63	0.062	10.0	100.9
Sb	8	4.95	0.33	0.067	5.0	99.1
Se	6	3.37	0.50	0.149	3.0	112.2
Sn	4	1.98	0.52	0.263	2.01	98.7
Sr	6[J]	2.01	0.04	0.019	2.01	100.2
Te	5	3.13	0.55	0.176	3.0	104.3

Element	No. Labs[E]	Mean(μg)	Std. Dev. (μg)[G]	RSD[I]	Reference value (μg)[H]	Recovery (%)
Ti	7	2.11	0.12	0.057	2.01	104.9
Tl	6	3.07	0.22	0.071	3.0	102.4
V	9	3.04	0.17	0.057	3.02	100.7
W	5	8.39	0.99	0.118	10.1	83.0
Y	5	2.03	0.08	0.038	2.01	100.8
Zn	9	5.23	0.31	0.060	5.2	100.6
Zr	5	2.03	0.13	0.062	2.01	101.2

[E]Number of laboratories reporting at least one result >MDL (or RL)

[G]standard deviation (if $p>1$);

[H]as reported by the CRM provider

[I]RSD: relative standard deviation

[J]excludes outlier (Grubbs' test)

TABLE IVc

Soluble capsules ILS mean values vs. certified reference values – Level 2

Element	No. Labs[E]	Mean (µg)	Std. Dev. (µg)[G]	RSD[I]	Reference value (µg)[H]	Recovery (%)
Ag	7	8.43	2.17	0.257	10.1	83.5
Al	7	29.6	0.91	0.031	30.9	95.7
As	8	20.8	1.11	0.053	20.2	103.0
Ba	7[J]	7.08	0.18	0.025	7.3	96.9
Be	9	7.05	0.48	0.068	7.0	100.7
Ca	8	161	23.55	0.147	165	97.4
Cd	9	7.05	0.28	0.040	7.0	100.7
Co	9	7.12	0.40	0.057	7.0	101.7
Cr	9	7.60	0.55	0.072	7.9	96.3
Cu	9	15.2	0.61	0.040	15.1	100.8
Fe	9	42.5	2.33	0.055	41.0	103.7
In	5	13.5	3.71	0.274	14.9	90.8
K	6	15.4	3.62	0.236	15.7	98.0
La	4	10.4	0.75	0.072	10.1	102.4
Li	7	6.64	0.46	0.070	7.0	94.9
Mg	7	27.5	2.51	0.091	27.9	98.7
Mn	9	7.03	0.43	0.061	7.0	100.4
Mo	9	7.27	0.35	0.048	7.1	102.4
Ni	9	7.26	0.54	0.074	7.0	103.7
P	6	25.7	2.29	0.089	24.9	103.1
Pb	9	25.3	1.35	0.053	25.2	100.4
Sb	9	24.9	1.42	0.057	25.1	99.0
Se	8	16.4	1.44	0.087	15.1	108.8
Sn	6	6.78	1.19	0.175	7.0	96.9
Sr	7	7.22	0.54	0.075	7.1	101.7
Te	5	13.0	1.00	0.077	12.6	102.8

Element	No. Labs[E]	Mean (µg)	Std. Dev. (µg)[G]	RSD[I]	Reference value (µg)[H]	Recovery (%)
Ti	7	7.07	0.73	0.104	7.0	101.0
Tl	7	10.1	0.58	0.058	10.1	99.6
V	9	7.12	0.44	0.062	7.0	101.7
W	5	24.5	2.81	0.115	25.1	97.6
Y	5	7.20	0.43	0.059	7.1	101.5
Zn	9	25.4	1.25	0.049	25.1	101.2
Zr	6	6.97	0.64	0.092	7.0	99.5

[E] Number of laboratories reporting at least one result >MDL (or RL)

[G] standard deviation (if $p>1$);

[H] as reported by the CRM provider

[I] RSD: relative standard deviation

[J] excludes outlier (Grubbs' test)

TABLE IVd

Soluble capsules ILS mean values vs. certified reference values – Level 3

Element	No. Labs[E]	Mean (μg)	Std. Dev. (μg)[G]	RSD[I]	Reference value (μg)[H]	Recovery (%)
Ag	7	13.7	7.07	0.515	20.1	68.2
Al	7	58.5	1.40	0.024	60.8	96.2
As	8	40.8	2.35	0.058	40.1	101.8
Ba	8	15.2	0.75	0.050	15.2	99.9
Be	9	14.9	0.76	0.051	14.9	100.1
Ca	8	206	26.71	0.130	215	95.8
Cd	8[J]	15.2	0.28	0.019	14.9	102.2
Co	9	15.2	0.87	0.058	14.9	102.0
Cr	9	15.4	0.55	0.035	15.8	97.2
Cu	9	30.0	0.96	0.032	29.9	100.2
Fe	9	83.1	4.50	0.054	80.5	103.2
In	5	34.2	11.09	0.324	39.7	86.2
K	6	21.9	4.37	0.199	20.7	105.8
La	4	20.1	1.58	0.079	20.1	99.9
Li	7	14.7	0.77	0.052	14.9	98.6
Mg	7	104	7.43	0.072	103	100.8
Mn	9	14.9	0.85	0.057	14.9	100.2
Mo	9	15.3	0.80	0.052	15.0	102.1
Ni	9	15.4	1.07	0.070	14.9	103.0
P	5[J]	101	1.75	0.017	99	102.2
Pb	9	100.	7.28	0.073	100	100.0
Sb	8[J]	40.2	1.45	0.036	40.2	100.0
Se	8	31.3	3.17	0.101	30.1	104.1
Sn	5[J]	15.3	0.76	0.050	14.9	102.8
Sr	7	15.1	0.92	0.061	15.0	100.9

Element	No. Labs[E]	Mean (µg)	Std. Dev. (µg)[G]	RSD[I]	Reference value (µg)[H]	Recovery (%)
Te	5	20.2	2.48	0.123	20.1	100.5
Ti	6[J]	15.4	0.52	0.034	14.9	103.2
Tl	7	19.8	1.48	0.075	20.1	98.3
V	9	15.2	0.89	0.058	14.9	101.9
W	5	38.7	6.35	0.164	40.2	96.4
Y	5	15.1	0.72	0.048	15.0	100.6
Zn	9	60.2	2.92	0.048	59.7	100.8
Zr	6	13.9	2.69	0.194	14.9	93.1

E number of laboratories reporting at least one result >MDL (or RL)

G standard deviation (if $p>1$);

H as reported by the CRM provider

I RSD: relative standard deviation

J excludes outlier (Grubbs' test)

TABLE V

Soluble capsules ILS – Estimates of bias, precision and accuracy

Element	Bias	n^K	$\check{S}^L$	$\hat{S}_{rT}{}^M$	Accuracy	$A_{U95}{}^N$
Ag	−0.18354	21	0.041	0.065	0.290	0.314
Al	−0.04141	21	0.006	0.050	0.124	0.143
As	0.01414	23	0.016	0.052	0.107	0.124
Ba	−0.02060	23	0.036	0.062	0.128	0.149
Be	0.00536	27	0.025	0.056	0.110	0.127
Ca	−0.03670	24	0.001	0.050	0.119	0.136
Cd	0.01327	26	0.022	0.055	0.111	0.127
Co	0.02376	27	0.036	0.062	0.129	0.149
Cr	−0.02808	26	0.046	0.068	0.144	0.166
Cu	0.00347	26	0.017	0.053	0.104	0.119
Fe	0.04756	27	0.011	0.051	0.132	0.148
In	−0.10293	15	0.056	0.075	0.226	0.260
K	−0.02388	17	0.029	0.058	0.123	0.147
La	0.01188	12	0.025	0.056	0.112	0.140
Li	−0.04467	21	0.039	0.064	0.149	0.173
Mg	−0.02193	21	0.012	0.051	0.109	0.128
Mn	0.00127	27	0.039	0.063	0.124	0.143
Mo	0.01690	27	0.032	0.060	0.121	0.140
Ni	0.04979	27	0.055	0.074	0.172	0.196
P	0.03096	16	0.010	0.051	0.115	0.137
Pb	0.00439	27	0.006	0.050	0.099	0.114
Sb	−0.00631	25	0.013	0.052	0.102	0.118
Se	0.08637	22	0.055	0.075	0.209	0.236
Sn	−0.00541	15	0.117	0.128	0.250	0.304
Sr	0.00930	20	0.011	0.051	0.102	0.120
Te	0.02560	15	0.063	0.081	0.166	0.201

Element	Bias	n [K]	$\breve{S}$ [L]	$\hat{S}_{rT}$ [M]	Accuracy	A_{U95} [N]
Ti	0.03046	20	0.032	0.059	0.131	0.154
Tl	0.00128	20	0.030	0.058	0.114	0.135
V	0.01433	27	0.020	0.054	0.109	0.126
W	−0.02395	15	0.010	0.051	0.110	0.134
Y	0.00971	15	0.020	0.054	0.107	0.130
Zn	0.00873	27	0.013	0.052	0.103	0.118
Zr	−0.02063	17	0.033	0.060	0.124	0.149

[K] number of reported results minus outliers (Grubbs' test, 1% confidence level)

[L] precision $\breve{S}$ =TRSD

[M] overall precision $\hat{\mathbf{S}}_{\mathbf{rT}} = \sqrt{\breve{S}^{2} + (0.05)^{2}}$

[N] upper 95% confidence limit of accuracy estimate